

**Appendix I**  
**Version With Markings To Show Changes Made**  
**in accordance with 37 C.F.R. § 1.121(c)(1)(ii)**

**In The Claims:**

Please cancel Claims 36-41 and 43-60.

Please amend the following Claims:

26. A method for detecting the presence of a target nucleic acid molecule [by detecting non-target cleavage products] comprising:
- a) forming a cleavage structure comprising: [providing:
    - i) a cleavage agent;]
    - [i]i) a synthetic target nucleic acid, said synthetic target nucleic acid comprising a first region and a second region, said second region downstream of and contiguous to said first region;
    - [i]ii) a first nucleic acid molecule [oligonucleotide], wherein at least a portion of said first nucleic acid molecule [oligonucleotide] is completely complementary to said first portion of said first target nucleic acid;
    - iii[v]) a second nucleic acid molecule [oligonucleotide] comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said second portion of said target nucleic acid;
  - b) cleaving said cleavage structure with a thermostable 5' nuclease so as to generate non-target cleavage product; and [mixing said cleavage agent, said synthetic target nucleic acid, said first oligonucleotide and said second oligonucleotide to create a reaction mixture under reaction conditions such that at least said portion of said first oligonucleotide is annealed to said first region of said target nucleic acid and wherein at least said 5' portion of said second oligonucleotide is annealed to said second region of said target nucleic acid so as to create a cleavage structure, and wherein cleavage of said cleavage structure occurs to generate non-target cleavage product; and]
  - c) detecting the cleavage of said cleavage structure.

Please add the following claims:

61. The method of Claim 26, wherein said cleaving step is conducted under isothermal conditions.

62. The method of Claim 26, wherein said thermostable 5' nuclease comprises a 5' nuclease of a DNA polymerase.

63. The method of Claim 62, wherein said DNA polymerase is *Taq* DNA polymerase.

64. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule comprises an aromatic ring.

65. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule comprises a 3' terminal nucleotide not complementary to said target nucleic acid.

66. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule consists of a single nucleotide.

67. The method of Claim 66, wherein said single nucleotide is not complementary to said target nucleic acid.

68. The method of Claim 66, wherein said single nucleotide is complementary to said target nucleic acid.

69. The method of Claim 65, wherein said 3' terminal nucleotide comprises a naturally occurring nucleotide.

70. The method of Claim 65, wherein said 3' terminal nucleotide comprises a nucleotide analog.

71. The method of Claim 26, wherein a plurality of said first nucleic acid molecule is provided, such that said first nucleic acid molecule is in concentration excess compared to said target nucleic acid.

72. The method of Claim 26, wherein a plurality of said second nucleic acid molecule is provided, such that said second nucleic acid molecule is in concentration excess compared to said target nucleic acid.

73. The method of Claim 26, wherein said target nucleic acid and said second nucleic acid form a duplex, and wherein a plurality of said first nucleic acid is provided such that said first nucleic acid molecule is in concentration excess compared to said duplex.

74. The method of Claim 73, wherein said cleaving said cleavage structure comprises cleaving said first nucleic acid molecule to generate non-target cleavage product.

75. The method of Claim 74, wherein said non-target cleavage product from said first nucleic acid molecule is generated in concentration excess compared to said duplex.

76. The method of Claim 26, further comprising providing a third nucleic acid molecule complementary to a third portion of said target nucleic acid upstream of said first portion of said first target nucleic acid, wherein said cleavage structure comprises said third nucleic acid molecule.

**Appendix II**  
**Entire Set Of Pending Claims**  
**pursuant to 37 C.F.R. § 1.121(c)(3)**

26. (Amended) A method for detecting the presence of a target nucleic acid molecule comprising:
- a) forming a cleavage structure comprising:
    - i) a synthetic target nucleic acid, said synthetic target nucleic acid comprising a first region and a second region, said second region downstream of and contiguous to said first region;
    - ii) a first nucleic acid molecule, wherein at least a portion of said first nucleic acid molecule is completely complementary to said first portion of said first target nucleic acid;
    - iii) a second nucleic acid molecule comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said second portion of said target nucleic acid;
  - b) cleaving said cleavage structure with a thermostable 5' nuclease so as to generate non-target cleavage product; and
  - c) detecting the cleavage of said cleavage structure.
27. The method of Claim 26, wherein said detecting the cleavage of said cleavage structure comprises detecting said non-target cleavage product.
28. The method of Claim 26, wherein said synthetic target nucleic acid comprises an amplified nucleic acid.
29. The method of Claim 28, wherein said amplified nucleic acid is produced using a polymerase chain reaction.
30. The method of Claim 26, wherein said detecting the cleavage of said cleavage structure comprises detection of fluorescence.

31. The method of Claim 26, wherein said detecting the cleavage of said cleavage structure comprises detection of mass.

32. The method of Claim 26, wherein said detecting the cleavage of said cleavage structure comprises detection of fluorescence energy transfer.

33. The method of Claim 26, wherein said detecting the cleavage of said cleavage structure comprises detection selected from the group consisting of detection of radioactivity, luminescence, phosphorescence, fluorescence polarization, and charge.

34. The method of Claim 26, wherein said first oligonucleotide is attached to a solid support.

35. The method of Claim 26, wherein said second oligonucleotide is attached to a solid support.

42. The method of Claim 26, wherein said synthetic target nucleic acid comprises DNA.

61. The method of Claim 26, wherein said cleaving step is conducted under isothermal conditions.

62. The method of Claim 26, wherein said thermostable 5' nuclease comprises a 5' nuclease of a DNA polymerase.

63. The method of Claim 62, wherein said DNA polymerase is *Taq* DNA polymerase.

64. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule comprises an aromatic ring.

65. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule comprises a 3' terminal nucleotide not complementary to said target nucleic acid.

66. The method of Claim 26, wherein said 3' portion of said second nucleic acid molecule consists of a single nucleotide.

67. The method of Claim 66, wherein said single nucleotide is not complementary to said target nucleic acid.

68. The method of Claim 66, wherein said single nucleotide is complementary to said target nucleic acid.

69. The method of Claim 65, wherein said 3' terminal nucleotide comprises a naturally occurring nucleotide.

70. The method of Claim 65, wherein said 3' terminal nucleotide comprises a nucleotide analog.

71. The method of Claim 26, wherein a plurality of said first nucleic acid molecule is provided, such that said first nucleic acid molecule is in concentration excess compared to said target nucleic acid.

72. The method of Claim 26, wherein a plurality of said second nucleic acid molecule is provided, such that said second nucleic acid molecule is in concentration excess compared to said target nucleic acid.

73. The method of Claim 26, wherein said target nucleic acid and said second nucleic acid form a duplex, and wherein a plurality of said first nucleic acid is provided such that said first nucleic acid molecule is in concentration excess compared to said duplex.

74. The method of Claim 73, wherein said cleaving said cleavage structure comprises cleaving said first nucleic acid molecule to generate non-target cleavage product.

75. The method of Claim 74, wherein said non-target cleavage product from said first nucleic acid molecule is generated in concentration excess compared to said duplex.

76. The method of Claim 26, further comprising providing a third nucleic acid molecule complementary to a third portion of said target nucleic acid upstream of said first portion of said first target nucleic acid, wherein said cleavage structure comprises said third nucleic acid molecule.

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Applicant: James R. PRUDENT *et al.*

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